

## SEQUENCE LISTING

<110> Merck & Co., Inc.  
Istituto di Ricerche di Biologia Molecolare P. Angeletti S.p.A.

<120> HCV REPLICONS CONTAINING NS5B FROM  
GENOTYPE 2B

<130> 21564Y PCT

<150> 60/517,605

<151> 2003-11-05

<160> 28

<170> FastSEQ for Windows Version 4.0

<210> 1

<211> 591

<212> PRT

<213> Artificial Sequence

<220>

<223> modified NS5B

<221> VARIANT

<222> (5)...(5)

<223> Xaa = threonine or serine

<221> VARIANT

<222> (24)...(24)

<223> Xaa = asparagine or serine

<221> VARIANT

<222> (31)...(31)

<223> Xaa = methionine or isoleucine

<221> VARIANT

<222> (376)...(376)

<223> Xaa = isoleucine or leucine

<400> 1

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Phe	His	Asn	Lys	Val	Tyr	Ser	Thr	Thr	Ser	Arg	Ser	Ala	Ser	Leu	Arg
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Ala	Lys	Lys	Val	Thr	Phe	Asp	Arg	Val	Gln	Val	Leu	Asp	Ala	His	Tyr
	50					55					60				
Asp	Ser	Val	Leu	Gln	Asp	Val	Lys	Arg	Ala	Ala	Ser	Lys	Val	Ser	Ala
65				70					75					80	
Arg	Leu	Leu	Thr	Val	Glu	Glu	Ala	Cys	Ala	Leu	Thr	Pro	Pro	His	Ser
			85						90					95	

Ala	Lys	Ser	Arg	Tyr	Gly	Phe	Gly	Ala	Lys	Glu	Val	Arg	Ser	Leu	Ser	100	105	110
Arg	Arg	Ala	Val	Asn	His	Ile	Arg	Ser	Val	Trp	Glu	Asp	Leu	Leu	Glu	115	120	125
Asp	Gln	His	Thr	Pro	Ile	Asp	Thr	Thr	Ile	Met	Ala	Lys	Asn	Glu	Val	130	135	140
Phe	Cys	Ile	Asp	Pro	Thr	Lys	Gly	Gly	Lys	Lys	Pro	Ala	Arg	Leu	Ile	145	150	155
Val	Tyr	Pro	Asp	Leu	Gly	Val	Arg	Val	Cys	Glu	Lys	Met	Ala	Leu	Tyr	165	170	175
Asp	Ile	Ala	Gln	Lys	Leu	Pro	Lys	Ala	Ile	Met	Gly	Pro	Ser	Tyr	Gly	180	185	190
Phe	Gln	Tyr	Ser	Pro	Ala	Glu	Arg	Val	Asp	Phe	Leu	Leu	Lys	Ala	Trp	195	200	205
Gly	Ser	Lys	Lys	Asp	Pro	Met	Gly	Phe	Ser	Tyr	Asp	Thr	Arg	Cys	Phe	210	215	220
Asp	Ser	Thr	Val	Thr	Glu	Arg	Asp	Ile	Arg	Thr	Glu	Glu	Ser	Ile	Tyr	225	230	235
Gln	Ala	Cys	Ser	Leu	Pro	Gln	Glu	Ala	Arg	Thr	Val	Ile	His	Ser	Leu	245	250	255
Thr	Glu	Arg	Leu	Tyr	Val	Gly	Gly	Pro	Met	Thr	Asn	Ser	Lys	Gly	Gln	260	265	270
Ser	Cys	Gly	Tyr	Arg	Arg	Cys	Arg	Ala	Ser	Gly	Val	Phe	Thr	Thr	Ser	275	280	285
Met	Gly	Asn	Thr	Met	Thr	Cys	Tyr	Ile	Lys	Ala	Leu	Ala	Ala	Cys	Lys	290	295	300
Ala	Ala	Gly	Ile	Val	Asp	Pro	Val	Met	Leu	Val	Cys	Gly	Asp	Asp	Leu	305	310	315
Val	Val	Ile	Ser	Glu	Ser	Gln	Gly	Asn	Glu	Glu	Asp	Glu	Arg	Asn	Leu	325	330	335
Arg	Ala	Phe	Thr	Glu	Ala	Met	Thr	Arg	Tyr	Ser	Ala	Pro	Pro	Gly	Asp	340	345	350
Leu	Pro	Arg	Pro	Glu	Tyr	Asp	Leu	Glu	Leu	Ile	Thr	Ser	Cys	Ser	Ser	355	360	365
Asn	Val	Ser	Val	Ala	Leu	Asp	Ser	Arg	Gly	Arg	Arg	Arg	Tyr	Phe	Leu	370	375	380
Thr	Arg	Asp	Pro	Thr	Thr	Pro	Xaa	Thr	Arg	Ala	Ala	Trp	Glu	Thr	Val	385	390	395
Arg	His	Ser	Pro	Val	Asn	Ser	Trp	Leu	Gly	Asn	Ile	Ile	Gln	Tyr	Ala	405	410	415
Pro	Thr	Ile	Trp	Val	Arg	Met	Val	Ile	Met	Thr	His	Phe	Phe	Ser	Ile	420	425	430
Leu	Leu	Ala	Gln	Asp	Thr	Leu	Asn	Gln	Asn	Leu	Asn	Phe	Glu	Met	Tyr	435	440	445
Gly	Ala	Val	Tyr	Ser	Val	Asn	Pro	Leu	Asp	Leu	Pro	Ala	Ile	Ile	Glu	450	455	460
Arg	Leu	His	Gly	Leu	Glu	Ala	Phe	Ser	Leu	His	Thr	Tyr	Ser	Pro	His	465	470	475
Glu	Leu	Ser	Arg	Val	Ala	Ala	Thr	Leu	Arg	Lys	Leu	Gly	Ala	Pro	Pro	485	490	495
Leu	Arg	Ala	Trp	Lys	Ser	Arg	Ala	Arg	Ala	Val	Arg	Ala	Ser	Leu	Ile	500	505	510
Ala	Gln	Gly	Ala	Arg	Ala	Ala	Ile	Cys	Gly	Arg	Tyr	Leu	Phe	Asn	Trp	515	520	525

Ala	Val	Lys	Thr	Lys	Leu	Lys	Leu	Thr	Pro	Leu	Pro	Glu	Ala	Ser	Arg
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Leu	Asp	Leu	Ser	Gly	Trp	Phe	Thr	Val	Gly	Ala	Gly	Gly	Gly	Asp	Ile
545					550					555					560
Tyr	His	Ser	Val	Ser	His	Ala	Arg	Pro	Arg	Leu	Leu	Leu	Leu	Cys	Leu
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<210> 2  
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 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> modified NS5B

<221> variation  
 <222> (3)...(3)  
 <223> n = A or T

<221> variation  
 <222> (9)...(9)  
 <223> n = C or A

<221> variation  
 <222> (13)...(13)  
 <223> n = A or T

<221> variation  
 <222> (15)...(15)  
 <223> n = A or C

<221> variation  
 <222> (21)...(21)  
 <223> n = A or G

<221> variation  
 <222> (24)...(24)  
 <223> n = C or G

<221> variation  
 <222> (28)...(28)  
 <223> n = T or C

<221> modified\_base  
 <222> (30)...(30)  
 <223> n = G or C

<221> variation  
 <222> (33)...(33)  
 <223> n = C or A

<221> variation  
 <222> (71)...(71)

<223> n = A or G

<221> variation

<222> (83)...(83)

<223> n = G or T

<221> variation

<222> (1174)...(1174)

<223> n = A or C

<400> 2

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gacgcacact	atgactcagt	cttgcaggac	gttaagcggg	ccgcctctaa	ggttagtgcg	240
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gtataccccc	accttgggggt	caggggtgtgc	gaaaagatgg	ccctctatga	catcgacaca	540
aagcttccca	aagcgataat	ggggccatcc	tatgggttcc	aatactctcc	cgcagaacgg	600
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gagggcagcc	gcctggattt	atccgggtgg	ttcaccgtgg	gcgcggcg	gggcgacatt	1680
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<210> 3

<211> 1394

<212> PRT

<213> Artificial Sequence

<220>

<223> modified NS3-5A

<221> VARIANT

<222> (1215)...(1215)

<223> Xaa = asparagine or serine

<221> VARIANT

&lt;222&gt; (904)...(904)

&lt;223&gt; Xaa = valine or alanine

&lt;400&gt; 3

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			20				25						30		
Glu	Val	Gln	Val	Val	Ser	Thr	Ala	Thr	Gln	Ser	Phe	Leu	Ala	Thr	Cys
		35					40					45			
Val	Asn	Gly	Val	Cys	Trp	Thr	Val	Tyr	His	Gly	Ala	Gly	Ser	Lys	Thr
	50					55				60					
Leu	Ala	Gly	Pro	Lys	Gly	Pro	Ile	Thr	Gln	Met	Tyr	Thr	Asn	Val	Asp
65					70					75					80
Gln	Asp	Leu	Val	Gly	Trp	Gln	Ala	Pro	Pro	Gly	Ala	Arg	Ser	Leu	Thr
				85					90					95	
Pro	Cys	Thr	Cys	Gly	Ser	Ser	Asp	Leu	Tyr	Leu	Val	Thr	Arg	His	Ala
			100					105					110		
Asp	Val	Ile	Pro	Val	Arg	Arg	Arg	Gly	Asp	Ser	Arg	Gly	Ser	Leu	Leu
		115					120					125			
Ser	Pro	Arg	Pro	Val	Ser	Tyr	Leu	Lys	Gly	Ser	Ser	Gly	Gly	Pro	Leu
	130					135					140				
Leu	Cys	Pro	Ser	Gly	His	Ala	Val	Gly	Ile	Phe	Arg	Ala	Ala	Val	Cys
145					150					155					160
Thr	Arg	Gly	Val	Ala	Lys	Ala	Val	Asp	Phe	Val	Pro	Val	Glu	Ser	Met
				165					170					175	
Glu	Thr	Thr	Met	Arg	Ser	Pro	Val	Phe	Thr	Asp	Asn	Ser	Ser	Pro	Pro
			180					185					190		
Ala	Val	Pro	Gln	Thr	Phe	Gln	Val	Ala	His	Leu	His	Ala	Pro	Thr	Gly
		195					200					205			
Ser	Gly	Lys	Ser	Thr	Lys	Val	Pro	Ala	Ala	Tyr	Ala	Ala	Gln	Gly	Tyr
	210					215					220				
Lys	Val	Leu	Val	Leu	Asn	Pro	Ser	Val	Ala	Ala	Thr	Leu	Gly	Phe	Gly
225					230					235					240
Ala	Tyr	Met	Ser	Lys	Ala	His	Gly	Ile	Asp	Pro	Asn	Ile	Arg	Thr	Gly
				245					250					255	
Val	Arg	Thr	Ile	Thr	Thr	Gly	Ala	Pro	Val	Thr	Tyr	Ser	Thr	Tyr	Gly
			260				265						270		
Lys	Phe	Leu	Ala	Asp	Gly	Gly	Cys	Ser	Gly	Gly	Ala	Tyr	Asp	Ile	Ile
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Ile	Cys	Asp	Glu	Cys	His	Ser	Thr	Asp	Ser	Thr	Thr	Ile	Leu	Gly	Ile
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Gly	Thr	Val	Leu	Asp	Gln	Ala	Glu	Thr	Ala	Gly	Ala	Arg	Leu	Val	Val
305					310					315					320
Leu	Ala	Thr	Ala	Thr	Pro	Pro	Gly	Ser	Val	Thr	Val	Pro	His	Pro	Asn
				325					330					335	
Ile	Glu	Glu	Val	Ala	Leu	Ser	Asn	Thr	Gly	Glu	Ile	Pro	Phe	Tyr	Gly
			340					345					350		
Lys	Ala	Ile	Pro	Ile	Glu	Ala	Ile	Arg	Gly	Gly	Arg	His	Leu	Ile	Phe
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Cys	His	Ser	Lys	Lys	Lys	Cys	Asp	Glu	Leu	Ala	Ala	Lys	Leu	Ser	Gly
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Leu	Gly	Ile	Asn	Ala	Val	Ala	Tyr	Tyr	Arg	Gly	Leu	Asp	Val	Ser	Val
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Ile	Pro	Thr	Ile	Gly	Asp	Val	Val	Val	Val	Ala	Thr	Asp	Ala	Leu	Met
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			420				425						430		
Val	Thr	Gln	Thr	Val	Asp	Phe	Ser	Leu	Asp	Pro	Thr	Phe	Thr	Ile	Glu
		435					440					445			
Thr	Thr	Thr	Val	Pro	Gln	Asp	Ala	Val	Ser	Arg	Ser	Gln	Arg	Arg	Gly
		450				455					460				
Arg	Thr	Gly	Arg	Gly	Arg	Met	Gly	Ile	Tyr	Arg	Phe	Val	Thr	Pro	Gly
465					470					475					480
Glu	Arg	Pro	Ser	Gly	Met	Phe	Asp	Ser	Ser	Val	Leu	Cys	Glu	Cys	Tyr
				485					490					495	
Asp	Ala	Gly	Cys	Ala	Trp	Tyr	Glu	Leu	Thr	Pro	Ala	Glu	Thr	Ser	Val
			500					505					510		
Arg	Leu	Arg	Ala	Tyr	Leu	Asn	Thr	Pro	Gly	Leu	Pro	Val	Cys	Gln	Asp
		515					520					525			
His	Leu	Glu	Phe	Trp	Glu	Ser	Val	Phe	Thr	Gly	Leu	Thr	His	Ile	Asp
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Ala	His	Phe	Leu	Ser	Gln	Thr	Lys	Gln	Ala	Gly	Asp	Asn	Phe	Pro	Tyr
545					550					555					560
Leu	Val	Ala	Tyr	Gln	Ala	Thr	Val	Cys	Ala	Arg	Ala	Gln	Ala	Pro	Pro
				565					570					575	
Pro	Ser	Trp	Asp	Gln	Met	Trp	Lys	Cys	Leu	Ile	Arg	Leu	Lys	Pro	Thr
			580					585					590		
Leu	His	Gly	Pro	Thr	Pro	Leu	Leu	Tyr	Arg	Leu	Gly	Ala	Val	Gln	Asn
		595					600					605			
Glu	Val	Thr	Leu	Thr	His	Pro	Ile	Thr	Lys	Tyr	Ile	Met	Ala	Cys	Met
	610					615					620				
Ser	Ala	Asp	Leu	Glu	Val	Val	Thr	Ser	Thr	Trp	Val	Leu	Val	Gly	Gly
625					630					635					640
Val	Leu	Ala	Ala	Leu	Ala	Ala	Tyr	Cys	Leu	Thr	Thr	Gly	Ser	Val	Val
				645					650					655	
Ile	Val	Gly	Arg	Ile	Ile	Leu	Ser	Gly	Arg	Pro	Ala	Ile	Val	Pro	Asp
			660					665					670		
Arg	Glu	Phe	Leu	Tyr	Gln	Glu	Phe	Asp	Glu	Met	Glu	Glu	Cys	Ala	Ser
		675					680					685			
His	Leu	Pro	Tyr	Ile	Glu	Gln	Gly	Met	Gln	Leu	Ala	Glu	Gln	Phe	Lys
	690					695					700				
Gln	Lys	Ala	Leu	Gly	Leu	Leu	Gln	Thr	Ala	Thr	Lys	Gln	Ala	Glu	Ala
705					710					715					720
Ala	Ala	Pro	Val	Val	Glu	Ser	Lys	Trp	Arg	Ala	Leu	Glu	Thr	Phe	Trp
				725					730					735	
Ala	Lys	His	Met	Trp	Asn	Phe	Ile	Ser	Gly	Ile	Gln	Tyr	Leu	Ala	Gly
			740					745					750		
Leu	Ser	Thr	Leu	Pro	Gly	Asn	Pro	Ala	Ile	Ala	Ser	Leu	Met	Ala	Phe
		755					760						765		
Thr	Ala	Ser	Ile	Thr	Ser	Pro	Leu	Thr	Thr	Gln	Ser	Thr	Leu	Leu	Phe
	770					775					780				
Asn	Ile	Leu	Gly	Gly	Trp	Val	Ala	Ala	Gln	Leu	Ala	Pro	Pro	Ser	Ala
785					790					795					800
Ala	Ser	Ala	Phe	Val	Gly	Ala	Gly	Ile	Ala	Gly	Ala	Ala	Val	Gly	Ser
			805						810					815	
Ile	Gly	Leu	Gly	Lys	Val	Leu	Val	Asp	Ile	Leu	Ala	Gly	Tyr	Gly	Ala
			820					825					830		



7/15

```

Arg Pro Asp Tyr Asn Pro Pro Leu Leu Glu Ser Trp Lys Asp Pro Asp
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Tyr Val Pro Pro Val Val His Gly Cys Pro Leu Pro Pro Ile Lys Ala
                      1285                      1290                      1295
Pro Pro Ile Pro Pro Pro Arg Arg Lys Arg Thr Val Val Leu Thr Glu
                      1300                      1305                      1310
Ser Ser Val Ser Ser Ala Leu Ala Glu Leu Ala Thr Lys Thr Phe Gly
                      1315                      1320                      1325
Ser Ser Glu Ser Ser Ala Val Asp Ser Gly Thr Ala Thr Ala Leu Pro
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Asp Gln Ala Ser Asp Asp Gly Asp Lys Gly Ser Asp Val Glu Ser Tyr
1345                      1350                      1355                      1360
Ser Ser Met Pro Pro Leu Glu Gly Glu Pro Gly Asp Pro Asp Leu Ser
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                      1380                      1385                      1390
Cys Cys

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<210> 4
<211> 4182
<212> DNA
<213> Artificial Sequence

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<220>
<223> modified NS3-5A

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<221> variation
<222> (2711)...(2711)
<223> n = T or C

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<221> variation
<222> (3645)...(3645)
<223> n = A or G

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gccacctac acgctcccac tggcagcggc aagagtacta aagtgccggc tgcataatgc 660
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gccctgtcta atactggaga gatccccttc tatggcaaag ccatcccatc tgaagccatc 1080
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Phe Trp Ala Lys His Met Trp Asn Phe Ile Ser Gly Ile Gln Tyr Leu
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65          70          75          80
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Cys	Ser	Thr	Pro	Cys											
			260												